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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,296	11/14/2003	Tinya Abrams	PC23579A	8864

28940 7590 04/15/2008

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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
04/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/712,296	ABRAMS ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed 11/30/07 presents remarks and arguments to the office action mailed 9/7/07. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 21-25 are now pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cancer, does not reasonably provide enablement for effective amount for preventing cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI

1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

In the instant case, on page 23, last 6 lines of the specification describes "therapeutically effective amount" as a capable of preventing.

Nature of the invention.

The nature of the invention is directed to preventing and or cure. As stated, however, claim 21 includes within its scope, preventing with a therapeutically effective amount. How can one prevent cancer in general. Multiple facts need to be address before one skilled in the art can contemplate on using the term prevention in any kind of way as these cancers can be genetic, acquired from the life style of the individual. One type of cancer is shown here that prevention is impossible.

State of the prior art and the predictability or lack thereof in the art.

The state of the prior art for example breast cancer is such that there is no sure way to prevent breast cancer. See American Cancer Society, (9/2007) underlined section. The existence of these obstacles establishes that the contemporary knowledge

in the art would prevent one of skill from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below:

Thus, in the absence of a showing how these compounds with a therapeutically effective amount are used for prevention one skilled in the art is unable to fully predict the nature of prevention from the administration of the compounds due to the unpredictability of the complexity of the disease.

Amount of direction and guidance provided by the inventor.

The amount of direction or guidance is not sufficient to claim preventing with the "therapeutically effective amount". The gap between the teaching in the specification of *in vitro* activity and *in vivo* is large enough to warrant thorough and compelling *in vivo* data especially in the absence of working examples demonstrating the full scope of treatment such as cure and prevention as described in the specification.

Existence of working examples.

As discussed above, the working example found in the specification in no way correlates to preventing with the therapeutically effective amount.

Claim Rejections - 35 USC § 103

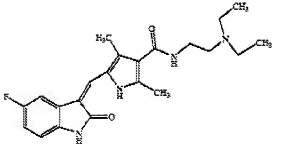
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-25 are rejected under 35 U.S.C. 103(a) as being obvious over Tang et al., US 6573293 (already of record) and Hawley et al, US2003/0069298 (IDS) in view of Goodman and Gilman, Pharm. 9th Ed. Pharmacological Basis of Therapeutics.

Tang et al. teach an indolinone, a tyrosine kinase inhibitor



5-(5-fluoro-2-oxo 1,2 dihydroindol-3-ylidenemethyl) -1H-pyrrole-3-carboxylic acid(2diethylaminoethyl)amide, is used for treating cancers such as colon, lung and breast cancer. See colabstract, col.70, col. 166, lines 10-11 and col. 252, lines 45-49. as required by instant claim 21 and 25.

Further, the reference teaches using these tyrosine inhibitors in a combination with other antimetabolite chemotherapy (see col. 175, lines 57-67), wherein daunorubicin and doxorubicin are used.

Hawley et al. teach the indole compound N-[2- (diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2- dihydro-2-oxo-3H-indol-3-ylidine)methyl]-2,4- dimethyl-IH-pyrrole-3-carboxamide, same as the compound of Tang et al with the same structure . See page 1, para 0006. The reference teaches the compound is used for treating breast cancer, lung cancer and can be combined with other chemotherapeutic agents such as 5-fluorouracil, cisplatin, daunorubicin, see page 8, para.s 0089-0092 as required by instant claims 21—23.

The combined reference fail to teach specific combination with irrinotecan and or docetaxel as required by instant claims 24-25.

However, the Hawley et al, reference teaches the combination of other chemotherapeutic agents such as alkaloids, see beginning of para 0089.

One of ordinary skill in the art would have been motivated to use other chemotherapeutic agents such as alkaloids and topoisomerase inhibitors based on the type of cancer rate of metastasis.

One of ordinary skill would have used the teachings suggested by Goodman and Gilman drawn to combination chemotherapy. See page 1225, Table X-1 and page 1230 with different classes of anticancer agents. One of ordinary skill in the art would have been motivated to combine the cited prior art of record disclosing the compound

of formula I, use with other known anti-cancer agents in claims 21-25, as suggested by Goodman and Gilman.

One of ordinary skill in the art would have been motivated to combine anticancer active agents, as taught by Goodman and Gilman, with the active compound to inhibit small cell lung cancer, breast etc because the combination for treating these cancers are taught in the prior art, and one of ordinary skill in the art would have expected a successful result from combining other well known anticancer agents that are known in the art for the same treatment.

No claim is allowed.

WO 03/016305 is cited as relevant art and is silent as the US publication is used in this instance (IDS).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
4/10/08

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614